Yescarta® (axicabtagene ciloleucel) Use in the Outpatient Setting

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The full indication, important safety information, and boxed warnings for cytokine release syndrome, neurologic toxicities and secondary hematological malignancies are available at:
https://www.gilead.com/-/media/files/pdfs/medicines/oncology/yescarta/yescarta-pi.

Summary

Kite cannot provide a specific recommendation regarding the administration of YESCARTA in an inpatient or outpatient setting. The healthcare provider should use their best clinical judgement to determine the appropriate site of care/administration of YESCARTA.

US Prescribing Information[1]

YESCARTA must be administered in a certified healthcare facility.

Patients should be monitored at least daily for 7 days at the certified healthcare facility following infusion for signs and symptoms of cytokine release syndrome (CRS) and neurologic toxicities. Patients should be instructed to remain within proximity of the certified healthcare facility for at least 4 weeks following infusion.

ZUMA-24 Study

- An ongoing, phase 2, open-label, multicenter study (ZUMA-24) is investigating outpatient use of axi-cel in relapsed/refractory large B-cell lymphoma (R/R LBCL) in adult patients. Patients received axi-cel 2 × 10^6 CAR T cells/kg along with prophylactic corticosteroid therapy. The primary endpoint was the incidence and severity of CRS and neurologic events (NEs). After a median follow-up of 7 months, all-grade and Grade ≥3 NEs were reported in 23/30 (77%) and 7/30 (23%) patients, respectively; all-grade CRS was reported in 27/30 (90%) patients; no patients experienced Grade ≥3 CRS. Hospitalization rate was 93% (28/30), and median time and duration of hospitalization were 4 and 8 days, respectively.[2]

This document provides an overview of emerging real-world evidence with outpatient management of patients administered axi-cel, with the intent to aid clinical decision making. The healthcare provider should use their best clinical judgement to determine the appropriate site of care/administration of axi-cel.

Real-World Evidence

- In a study of 116 patients who received outpatient administration of axi-cel at the Mayo Clinic, 103/116 (89%) were admitted for inpatient care within 30 after the infusion. All-grade/Grade ≥3 CRS and ICANS were reported in 83%/3% and 51%/17% patients within 30 days following infusion, respectively.[3]
- In a report of 64 patients who received outpatient administration of chimeric antigen receptor (CAR) T-cell therapy at the Mayo Clinic, including axi-cel, 59 (92.2%) were eventually admitted for inpatient care at a median of 2 days after the infusion. Remote patient monitoring (RPM) data was collected to monitor patients in an outpatient setting and potentially identify concerns outside of scheduled follow-up. Of the 19 patients enrolled in RPM and receiving CAR T-cell therapy, 17 had evaluable RPM data. Of these, 14 patients eventually required admission.[4]
- In another analysis of 39 patients who received outpatient dosing of CAR-T therapy at the Mayo Clinic, 32 patients were admitted at a median of 1 day after the infusion. Of the 8 patients who received axi-cel, 7 received outpatient dosing, and 6 were admitted (including 2 within 3 days after infusion).[5]
- Outcomes in 143 patients with DLBCL, infused with axi-cel in either the inpatient or outpatient setting were studied across 5 transplant and cell therapy centers in the US. The ORR at Day 30 post-axi-cel infusion was achieve in 76% and 70% of outpatient and inpatient cases, respectively. The median PFS observed in the outpatient group was significantly higher than the inpatient cohort (not reached vs 365 days, P=0.033). There was no significant difference in the median OS for the outpatient cohort compared to inpatient. The incidence of CRS and ICANS was 85% (11% Grade ≥3) and 49% (18% Grade ≥3), respectively. Six (13%) of the outpatient treated patients avoided subsequent hospitalization and the outpatient and inpatient cohorts had similar ICU rates (28% vs. 23%) and median ICU LOS (8 vs 5 days, P=0.3). Median hospital LOS for the outpatient group was 8 days compared to 15 days for the inpatient group (P<0.001).[6]
- In a retrospective single-center cohort study of 20 patients treated with outpatient CAR T-cell therapy, no patients were admitted in the first 72 hours post infusion, while 10 were admitted within the first month of therapy. Of the 3 patients who received axi-cel, 2 were admitted (both >72 hours post-infusion).[7]
- In a study conducted at Vanderbilt University Medical center, axi-cel was administered on an outpatient basis to 9 patients, with 2 weeks of telemedicine monitoring after the infusion. Patient had to have minimal comorbidities and a reliable caregiver to be eligible for this protocol; >90% had Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1. No admission was required for 3 (23%) of the 13 patients in an overall CAR T cohort.[8]
- Outcomes in 13 patients who received outpatient administration of axi-cel were described in a report from University of Oklahoma Health Sciences Center, with established post-infusion monitoring practices (visits daily for 2 weeks then thrice-weekly for 2 weeks). There were 10 admissions (76%) by Day 30, all attributed to fever.[9]

- Outcomes in 47 patients who received outpatient administration of CAR-T therapy (including 29 patients who received axi-cel) were described in a report from Johns Hopkins University Hospital. After a median follow-up of 364 days, hospitalization rates were 12/14 (86%) in patients aged ≥65 years and 27/33 (82%) in those aged <65 years. Of patients who received axi-cel, all-grade and Grade ≥3 ICANS were reported in 8/14 (57%) and 4/14 (29%) patients aged ≥65 years and in 6/22 (27%) and 3/22 (14%) patients aged <65 years, respectively.[10]
- A multicenter, real-world study of 20 patients with R/R LBCL receiving axi-cel as an outpatient infusion was conducted. All patients required admission at median day 1. No additional information related to toxicity management or monitoring was reported.[11]

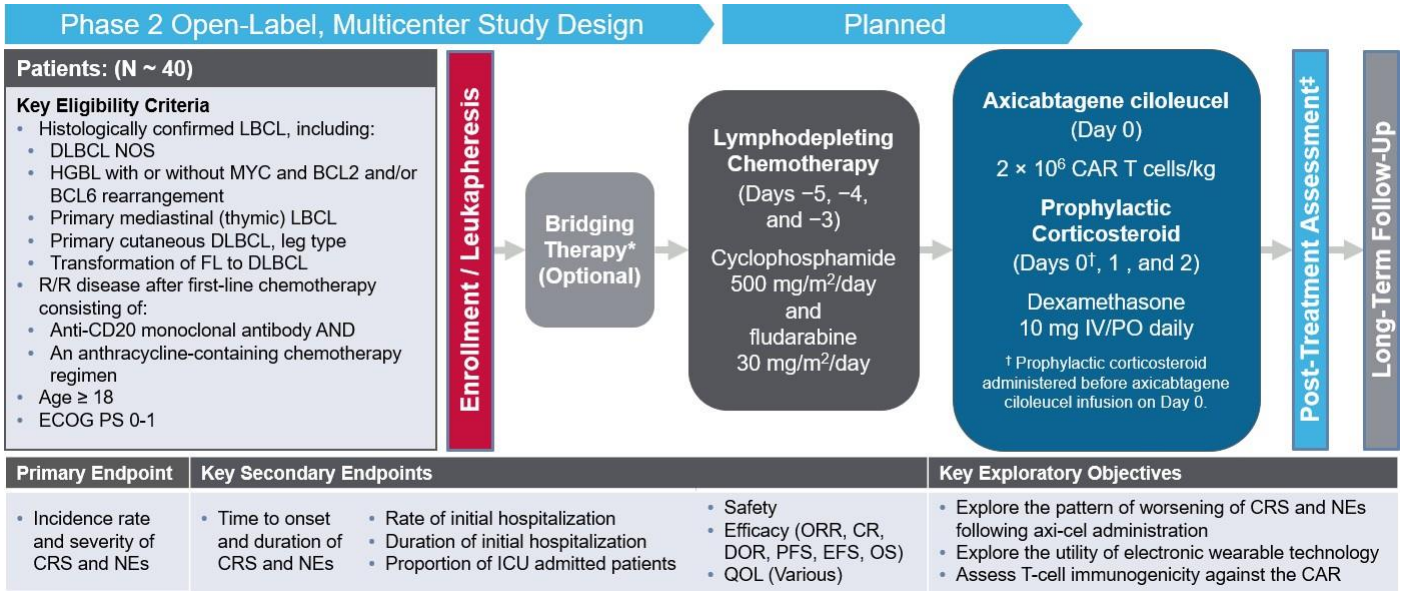
Clinical Studies

ZUMA-24

Study Design and Patients

An ongoing, Phase 2, open-label, multicenter study (ZUMA-24; NCT05459571) evaluated the outpatient use of axi-cel in R/R LBCL in 30 adult patients. Patients received lymphodepleting chemotherapy between leukapheresis and axi-cel infusion. Axi-cel was administered at a dose of 2 × 10^6 CAR T cells/kg along with prophylactic corticosteroid therapy. Inclusion criteria and other details of the study plan are depicted in Figure 1.[2,12]

Figure 1. Study Design of Ongoing ZUMA-24 Study[12]



CAR=chimeric antigen receptor; CR=complete response; CRS=cytokine release syndrome; DLBCL=diffuse large B-cell lymphoma; DOR=duration of response; ECOG=Eastern Cooperative Oncology Group; EFS=event free survival; FL=follicular lymphoma; HGBL=high-grade B-cell lymphoma; IV=intravenous; LBCL=large B cell lymphoma; NE=neurologic event; NOS=not otherwise specified; ORR=objective response rate; OS=overall survival; PFS=progression free survival; PO=by mouth; PS=performance status; QOL=quality of life; R/R=relapsed/refractory.
*Bridging therapy after leukapheresis is at the discretion of the investigator and will be administered in the 7 days before lymphodepleting chemotherapy.

Selected baseline characteristics of the population of 30 patients who received treatment with axi-cel are summarized in Table 1.[2]

Table 1. Baseline Characteristics[2]

Characteristic	Treated with Axi-cel (N=30)
Age, years, median (range)	62 (24–76)
Age ≥65 years, n (%)	11 (37)
Male, n (%)	20 (67)
Ann Arbor Stage III/IV, n (%)	5 (17)/4 (47)
ECOG performance status 1, n (%)	10 (33)
Disease type, n (%)	
DLBCL not otherwise specified	24 (80)
HGBL with or without *MYC* and *BCL2* and/or *BCL6* rearrangement	1 (3)
PMBCL	2 (7)
TFL	3 (10)
IPI score, n (%)	
0-1	25 (83)
2	2 (7)
4	1 (3)
Prior lines of chemotherapy, n (%)	
1	28 (93)
2	2 (7)
LDH at baseline, U/L, median (range)	198 (102-1136)
Tumor SPD, mm^2, median (range)	2348 (221–17,843)

DLBCL=diffuse large B-cell lymphoma; ECOG=Eastern Cooperative Oncology Group; HGBL, high-grade B-cell lymphoma; IPI=International Prognostic Index; LDH=lactate dehydrogenase; PMBCL= primary mediastinal B-cell lymphoma; SPD=sum of the products of the diameters; TFL=transformed follicular lymphoma.

Following axi-cel infusion at the study site, patients were monitored daily for 7 days at an outpatient healthcare facility. Patients were required to remain within 2 hours of the study site for at least 4 weeks following axi-cel infusion. Criteria for hospitalization included CRS and NEs, and other events according to the discretion of the physician.[2]

The primary endpoint was the incidence and severity of CRS and NEs. Time to onset and duration of these events were investigated as key secondary endpoints. Additional select secondary endpoints included the rate and duration of initial hospitalization, the proportion of patients admitted to intensive care units, and efficacy, safety, and quality-of-life endpoints.[2,12]

Outcomes

As of April 5, 2024, 30 patients treated with CAR-T were followed for a median of 7 months (range, 1–18 months). CRS developed in 90% of patients (n=27) with a median duration of 5 days (range, 3–6 days). All CRS events of were Grade 1 or Grade 2 (37% and 53% of patients; respectively). Twenty-three patients (77%) developed NEs; events were primarily Grades 1–3 in severity, with 1 Grade 4 event and no Grade 5 events. Safety outcomes are summarized in Table 2.[2]

Table 2. Safety Outcomes[2]

Detail/Event	Outpatients Treated with Axi-cel (N=30)
Outpatients hospitalized after infusion, n (%)	28 (93)
Time to first hospitalization, days, median (range)	4 (2–9)
Duration of first hospitalization, days, median (range)	8 (2–44)
ICU admission, n (%)	4 (13)
CRS, n (%)	27 (90)
Grade 1	11 (37)
Grade 2	16 (53)
Grade 3	0
Grade 4	0
Grade 5	0
Time from infusion to CRS, days, median (range)	4 (not estimable–not estimable)
Duration of CRS, days, median (range)	5 (3–6)
Tocilizumab use for CRS, n (%)	26 (87)
Steroid use for CRS, n (%)	9 (30)
NEs, n (%)	23 (77)
Grade 1	8 (27)
Grade 2	8 (27)
Grade 3	6 (20)
Grade 4	1 (3)
Grade 5	0
Time from infusion to NEs, days, median (range)	7 (6–14)
Duration of NEs, days, median (range)	6 (3–13)
Tocilizumab use for NEs, n (%)	0
Steroid use for NEs, n (%)	13 (43)

CRS=cytokine release syndrome; ICU=intensive care unit; NE=neurologic event.

Grade ≥3 AEs (most commonly reported: neutrophil count decreased [n=12] and WBC count decreased [n=9]) and SAEs (most commonly reported: neutropenia [n=16] and thrombocytopenia [n=6]) each occurred in 80% of patients. There were no Grade 5 AEs.[2]

The objective response rate was 83% (95% CI, 65%–94%) and the complete response rate was 67% (95% CI, 47%–83%). The study is ongoing and the primary analysis results will be reported at a later date.[2]

Real-World Evidence

Experience From a Single Center Hospital-Based Outpatient (HBO) Practice (Mayo Clinic)[3,4,5]

Study Design and Patients[3]

Bansal, et al. (2024) reported real-world outpatient administration of axi-cel and brexucabtagene autoleucel (brexu-cel) at the Mayo Clinic in 155 patients with R/R non-Hodgkin lymphoma (NHL) who received treatment between January 2018 and December 2022 and had follow-up through

November 2023. Outcomes of interest included incidence of CRS and ICANS, hospital resource utilization rates and effectiveness outcomes (DOR, PFS, and OS). Outcomes were also evaluated according to early management period (EMP; earlier intervention [corticosteroid and tocilizumab intervention, and use of levetiracetam prophylaxis] to treat AEs) vs late management period (LMP; later intervention to treat AEs).[3]

Outcomes

A total of 116 patients with LBCL received outpatient axi-cel treatment (EMP, n=25; LMP, n=91). Overall, patients had a median age of 60 years and 66% (n=76) were male; 95% (n=110) had an ECOG performance status of 0–1, and 69% (n=80) had ≥3 prior lines of therapy. CRS developed in 83% of patients (n=96), including 3 reports (3%) of Grade ≥3 CRS. The median time to onset of initial CRS was 4 days following infusion. Fifty-nine patients (51%) developed ICANS, including 17% (n=20) with Grade ≥3 events. Details of CRS and ICANS events, as well as hospitalizations, are summarized in Table 3.[3]

Table 3. Safety Outcomes in Patients with LBCL Treated with Outpatient Axi-Cel[3]

Detail/Event		EMP (n=25)	LMP (n=91)	*P*-value	Overall (N=116)
Hospital Utilization	Any early hospitalization (≤3 days post-infusion), n (%)	7 (28)	40 (44)	0.15	47 (41)
	Any hospitalization (≤30 days post-infusion), n (%)	20 (80)	83 (91)	0.15	103 (89)
	Duration of first hospitalization, days, median (IQR)	7 (4.5-9.5)	10 (5-12)	0.08	9 (5–12)
	Any ICU admission (≤30 days post-infusion), n (%)	0 (0)	21 (23)	0.006	21 (18)
	Duration of ICU stay, days, median (IQR)	0 (0)	4 (2-5)	N/A	4 (2–5)
	Tocilizumab use, n (%)	7 (100)	19 (48)	0.012	26 (55)
	Corticosteroid use, n (%)	0 (0)	7 (18)	0.573	7 (15)
CRS	Initial CRS (≤30 days after infusion), n (%)	19 (76)	77 (85)	0.371	96 (83)
	Grade ≥3	0 (0)	3 (3)	0.784	3 (3)
	Time to onset of initial CRS, days, median (range)	4 (2-6)	4 (2-6)	0.447	4 (2–6)
	Time to resolution of initial CRS, days, median (range)	4 (3-6)	5 (3-8)	0.039	5 (3–7)
ICANS	Initial ICANS (≤30 days after infusion), n (%)	10 (40)	49 (54)	0.222	59 (51)
	Grade ≥3	5 (20)	15 (16)	0.595	20 (17)
	Time to onset of initial ICANS, days, median (range)	6 (6-8)	7 (5-8)	0.878	6 (5–8)
	Time to resolution of initial ICANS, days, median (range)	4.5 (3-6)	5 (3-9)	0.422	5 (3–9)

CRS=cytokine release syndrome; EMP, early management period (Nov 2021–Dec 2022); IQR=interquartile range; LMP, late management period (Jan 2018–Oct 2021); N/A=not available; NE=neurologic event.

Outcomes were similar in the EMP and LMP cohorts, with the exceptions of median time to CRS resolution (4 vs 5 days; *P*=0.039), use of tocilizumab within 3 days following infusion (100% vs 48%; *P*=0.012), and ICU admission within 30 days (0% vs 23%; *P*=0.006), respectively.[3]

At a median follow-up of 16.5 and 41 months in the EMP and LMP cohorts, best overall response rates were 88% (CR, 84%) and 76% (CR, 59%) in the EMP and LMP cohorts, respectively. Median DOR, PFS, and OS were 12.9, 4.3, and 22.5 months, respectively, in the LMP cohort and not reached in the EMP cohort.[3]

Study Design and Patients[4]

Bansal, et al. (2021) described a treatment protocol at the Mayo Clinic in patients with aggressive lymphoma who received CAR-T therapy; 64 of the patients received outpatient

administration. The patients who received CAR-T on an outpatient basis were allowed to opt for remote patient monitoring.

For the first 7 days after the CAR T infusions, the patients had daily visits. After Day 7, visits were conducted depending on the patient's medical need, and remote patient monitoring was used for those who had enrolled. The hospital-based outpatient practice monitored those who had enrolled for remote patient monitoring daily with assessments of vital signs and symptoms 4 times a day, with additional assessments performed if the patient's condition or new symptoms warranted. Alerts were recorded in case of vital signs or patient symptoms of concern.

Patients were admitted for inpatient care for any of the following:

- Fever (body temperature ≥38.3°C)
- Unstable vital signs
- Elevations in C-reactive protein
- Development of neurologic symptoms
- Clinical concerns

Outcomes[4]

Of the 64 patients (89%) who received outpatient CAR T in the Mayo Clinic, 59 (92.2%) were admitted to inpatient care at a median of 2 days (range, 0–25 days) after the infusion; their median length of hospital stay for the first admission was 8 days (range, 1–27 days). Significant associations (P<0.01) were determined between early admission and administration of bridging therapy and elevations in C-reactive protein and lactate dehydrogenase. A second admission was required for 14 patients at a median of 13.5 days, and a third admission was required for 4 patients at a median of 28 days. Median length of stay was 3 days for both the second and third admission.

Remote patient monitoring was used for 19 of the patients, 16 of whom received axi-cel. Data from remote patient monitoring were available for 17 patients. Of those monitored remotely, 14 patients required ≥1 admission, for a total of 17 admissions. Of these admissions, 16 were based on alerts from remote monitoring. In the 48 hours preceding each admission, there were a median of 2 alerts (range, 0–10). Alerts were primarily for vital signs, including body temperature (19 alerts, 11 admissions), oxygen saturation (16 alerts, 6 admissions), and heart rate (14 alerts, 5 admissions); these were also the alerts that led to the most admissions in the subsequent 48 hours.

After inpatient admissions, subsequent interventions occurred a median of 2 days later and included administration of tocilizumab (n=8), vasopressors (n=1), or steroids (n=1); oxygen support (n=4); and transfer to intensive care (n=3).

Study Design and Patients[5]

In another report of the safety and feasibility of HBO management of patients who received CAR-T therapies at the Mayo Clinic, Bansal, et al. (2022) evaluated outcomes from a retrospective analysis of patients treated from March 2021 to June 2022. CAR-T therapies included axi-cel for follicular lymphoma (FL) (Grade 1–3A) (n=8), brexu-cel for mantle cell lymphoma (MCL) (n=10), and anti-B-cell maturation antigen (BCMA) CAR-T therapies (idecabtagene vicleucel and ciltacabtagene autoleucel) for multiple myeloma (MM) (n=32).

Patients received CAR-T treatment at the HBO unit and were then monitored daily for 7 days. After Day 7, visits were conducted as clinically needed until criteria for admission (including fever, elevated C-reactive protein, or new neurologic symptoms) were met.

Outcomes[5]

Patients (n=50) had a median age of 65 years (range 44–89), and 54% (27) were male. At baseline, 1 patient (2%) had an ECOG performance score of 2 or greater, and most (76%) underwent prior ASCT. Patients had a median of 5 (range, 2–13) prior lines of therapy.

Of the 50 CAR T patients, 39 (78%) received outpatient dosing, of which 7 (18%) were not admitted. Of the 32 patients who were admitted, the median time to first admission was 1 day (range, 0–9) and the median duration of hospital stay was 6 days (range, 2–49). The most common criteria for hospitalization was fever (79%; n=25).

Of the 8 patients who received axi-cel, 7 (87.5%) received outpatient dosing, and 6 (75%) were admitted, including 2 with early (≤3 days post infusion) admission and 4 with late admission. Median time to admission was 6 days (range, 1–9) and the median duration of hospital stay was 7.5 days (range, 5–12).

After inpatient admissions, subsequent interventions occurred at a median of 1 day later and included administration of tocilizumab (81%; n=26/32), steroid (3%; n=1/31), escalation of oxygen support (12.5%; n=4/32), vasopressor (3%; n=1/32), ventilator (3%; n=1/32), hemodialysis (3%; n=1/32), and ICU transfer (9%; n=3/32).

Multicenter Study from Sarah Cannon Cancer Network[6]

Study Design and Patients

Battiwalla, et al. assessed the outcomes in 167 patients, including 143 (86%) patients with DLBCL and 24 (14%) with FL, infused with axi-cel in either the inpatient or outpatient setting, supported by remote monitoring, across 5 transplant and cell therapy centers in the US. The results focus on patients with DLBCL treated with axi-cel.

Outcomes

Axi-cel was mainly administered as 2nd or 3rd line of treatment in DLBCL (~70%). Forty seven of the 143 patients were infused in the outpatient setting and showed a similar time from referral to infusion, compared to the inpatient cohort (111 vs 95 days, P=0.10). Bendamustine was administered to 57% of the outpatient and 7% of inpatient, whereas conditioning with Flu/Cy was used in 43% of outpatient and 71% of inpatient treated patients (Table 1).

The median follow up for the overall DLBCL, outpatient and inpatient cohorts was 419, 383 and 461 Days, respectively.

Table 1. Baseline Demographics[6]

Characteristics	Inpatient (n=96)	Outpatient (n=47)	DLBCL Overall (N=143)
Male, n (%)	54 (56)	29 (62)	83 (58)
Median Age (range), years	60 (24-78)	65 (25-80)	61 (24-80)
Prior ASCT, n (%)	11 (11)	5 (11)	16 (11)
CAR T Line of Therapy, n (%)			
2L	36 (38)	22 (46)	58 (41)
≥3L	54 (56)	23 (49)	77 (54)
Lymphodepleting Regimen, n (%)			
Bendamustine	7 (7.3)	27 (57)	34 (24)
Flu/Cy	68 (71)	20 (43)	88 (62)
Prophylactic dexamethasone, n (%)	16 (17)	42 (89)	58 (41%)

ASCT=autologous stem cell transplantation; CAR=chimeric antigen receptor; DLBCL=diffuse large B-cell lymphoma; Flu/Cy=fludarabine/cyclophosphamide

The ORR (CR + PR) at Day 30 post-axi-cel infusion was achieve in 76% and 70% of outpatient and inpatient cases, respectively (Table 2).

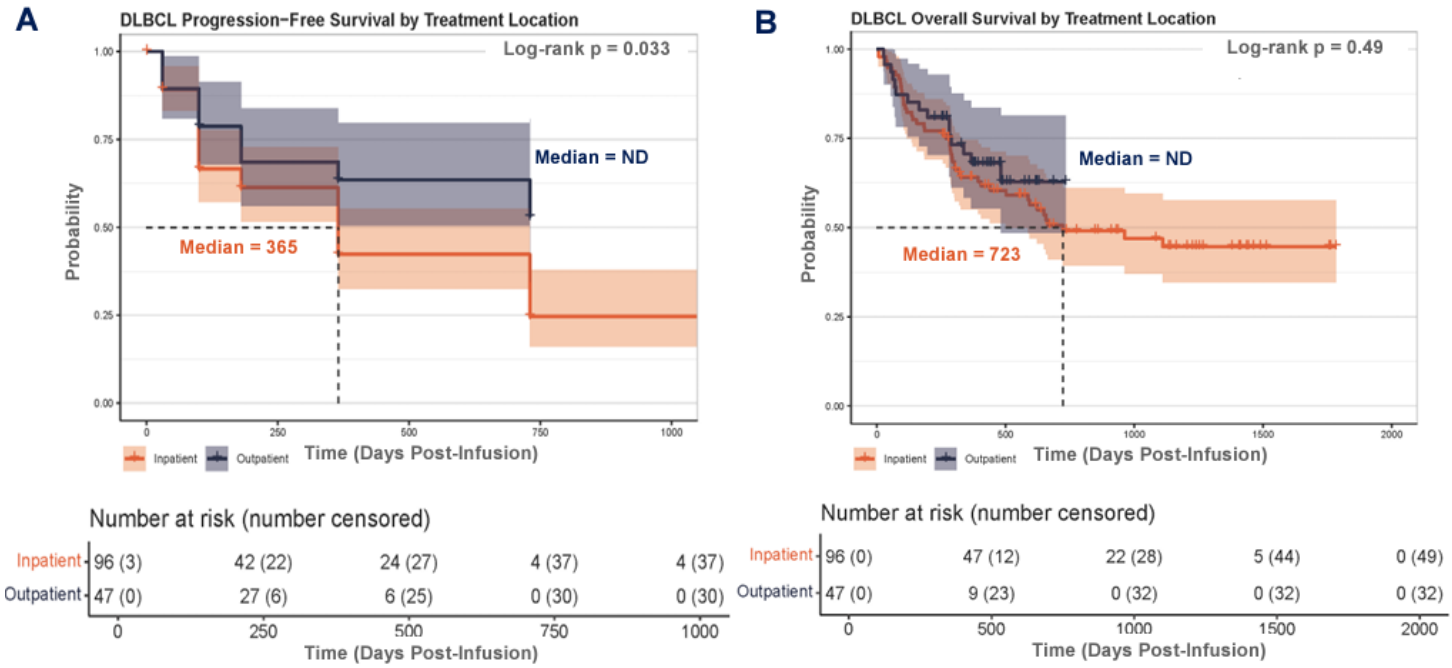
Table 2. Efficacy and Safety Outcomes[6]

Characteristics	Inpatient (n=96)	Outpatient (n=47)	DLBCL Overall (N=143)
ORR[a], n (%)	45 (70)	34 (76)	79 (72)
CR[a]	31 (32)	21 (45)	52 (36)
PR[a]	14 (15)	13 (28)	27 (19)
PD[a]	10 (10)	4 (8.5)	14 (9.8)
CRS, n (%)			
Any Grade	82 (85)	39 (83)	121 (85)
Grade ≥3	13 (14)	3 (6.4)	16 (11)
ICANS, n (%)			
Any Grade	54 (56)	16 (34)	70 (49)
Grade ≥3	23 (24)	3 (6.4)	26 (18)
Median cumulative reactive dexamethasone dose, mg (IQR)	207 (104-308)	70 (30-248)	142 (60-299)
Received, n (%)			
tocilizumab[b]	59 (61)	35 (74)	94 (66)
anakinra[c]	3 (3.1)	4 (8.5)	7 (4.9)
Hospitalisation, n (%)	96 (100)	41 (87)	137 (96)
LOS, days (IQR)	15 (11-21)	8 (4-12)	13 (9-18)
ICU admission, n (%)	22 (23)	13 (28)	35 (24)
LOS, days (IQR)	5 (2-10)	8 (4-12)	8 (2-12)
Death, n (%)	47 (49)	15 (32)	62 (43)

[a] At Day 30.
[b] Administered for CRS.
[c] Administered for steroid refractory ICANS
CR=complete response; CRS=cytokine release syndrome; DLBCL=diffuse large B-cell lymphoma; ICANS=immune cell effector associated neurotoxicity syndrome; ICU=intensive care unit; IQR=interquartile range; LOS=length of stay; ORR=objective response rate; PD=progressive disease; PR=partial response

The median PFS observed in patients treated in the outpatient setting was significantly higher than those treated in inpatient setting (not reached vs 365 days, *P*=0.033). There was no significant difference in the median OS for the outpatient cohort compared to inpatient (not reached vs 723 days, *P*=0.49) (Figure 2).

Figure 2. Progression-Free Survival[a] (A) and Overall Survival (B) Curves[6]



[a] PFS includes death from all causes as an event, along with progression (death is not treated as censor).
DLBCL=diffuse large B-cell lymphoma; OS=overall survival; PFS=progression-free survival.

Prophylactic dexamethasone was administered more frequently in the outpatient vs inpatient cohort (89% vs. 17%), but with no significant impact on the time to onset of CRS (4 vs 4 days, *P*=0.2) or ICANS (6 vs 5 days, *P*=0.2).

The incidence of CRS was 85% (11% Grade ≥3) and the incidence of ICANS was 49% (18% Grade ≥3). The median cumulative reactive dexamethasone dose administered to patients treated in the outpatient setting was less than 50% of that administered to inpatient treated subjects (70 vs 207 mg). The corresponding use of tocilizumab for CRS was 66%, and anakinra for steroid refractory ICANS was 4.9%.

Six (13%) of the patients treated in the outpatient setting avoided subsequent hospitalization and the outpatient cohort had similar ICU rates (28% vs. 23%) to those treated in the inpatient setting.

Median length of stay (LOS) for the outpatient group was 8 days compared to 15 days for the inpatient group (*P*<0.001), with no difference in median intensive care unit (ICU) LOS for those admitted to ICU (8 vs 5 days, *P*=0.3).

Retrospective Single-Center Cohort Study[7]

Study Design and Patients

Kirby, et al. reported outcomes from a retrospective single-center cohort study of 20 patients treated with outpatient CAR T-cell therapy between February 2021 and March 2022. All patients had at least 100 days of post-infusion follow up and were monitored in an outpatient setting with daily triage visits with a registered nurse and twice weekly visits to an advanced practice provider or physician. No remote monitoring devices were used; patients and caregivers were instructed to report any CRS or neurologic toxicities to a 24-hour on-call advanced practice provider/physician.

CAR-T treatments included axi-cel (n=3), tisagenlecleucel (n=2), lisocabtagene maraleucel (n=14), and brexucabtagene autoleucel (n=1). Patients had a median age of 69.5 years (range 46–81), and 60% were male. Prophylactic dexamethasone had been administered to 65% of patients. At baseline, 55% of patients had an IPI score of 3–4, and 25% had an ECOG score of 2 or greater.

Outcomes

Of the 20 patients in the cohort, no patients were admitted in the first 72 hours post infusion, and 10 (50%) were admitted within the first month of therapy (CRS was the initial reason for admission in all cases). Grade ≥3 CRS and neurologic toxicities were reported in 5% and 20% of patients, respectively. Two patients died within 30 days post-treatment, due to causes that were considered unlikely related to outpatient monitoring (progressive disease and methicillin-resistant *Staphylococcus aureus* bacteremia). At 6 months and 1 year, progression-free survival rates were 65% and 60% and overall survival were 85% and 75%, respectively.

Of the 3 patients who received axi-cel, 2 were admitted >72 hours post-infusion; 1 patient had Grade ≥3 CRS and 2 had Grade ≥3 neurologic toxicities. All 3 patients received prophylactic steroid therapy.

Vanderbilt University Medical Center study[8]

Study Design and Patients

Dholaria, et al. described outpatient administration of axi-cel to 9 patients at Vanderbilt University Medical Center for R/R LBCL. Patients were eligible for this protocol if they met criteria from ZUMA-1 and had minimal comorbidities, a reliable caregiver, and baseline tumor sum of the products of diameters (SPD) <1000 mm^2. Selected baseline characteristics of the population of 13 patients who received axi-cel (n=9) or other CAR-T therapy are in Table 4.

Table 4. Baseline Characteristics[8]

Characteristic	Outpatients Treated with Axi-cel or Other CAR-T (N=13)
Age, years, median (range)	64 (44–70)
Age ≥65 years, n	6
Male	11 (84.6)
Ann Arbor Stage III–IV, n (%)	10 (77)
ECOG performance status, n (%)	
0	4 (30.8)
1	8 (61.5)
2	1 (7.7)
IPI score, n (%)	
0-2	4 (44.4)
3-4	9 (55.6)
Prior lines of therapy	
Median, n (range)	3 (2–5)
2, n (%)	3 (23.1)
3, n (%)	5 (38.5)
≥4, n (%)	4 (30.8)
Prior autologous transplant, n (%)	4 (30.8)
Bridging therapy, n (%)	7 (54)
Pre-lymphodepletion LDH, U/L, median (range)	252 (152-349)
Pre-lymphodepletion ferritin, ng/mL, median (range)	992 (308–4232)
Primary refractory disease, n (%)	8 (62)
Tumor SPD, mm^2, median (range)	923 (28–8568)

ECOG=Eastern Cooperative Oncology Group; IPI=International Prognostic Index; SPD=sum of the products of the diameters.

After administration of lymphodepleting chemotherapy and CAR T infusion, the patients were monitored for 14 days, with visits in person twice daily and 1 overnight visit conducted remotely via telemedicine. The caregivers received training in the use of devices to facilitate telemedicine, and patients and caregivers both received training on monitoring for vital signs, CRS, and ICANS. Caregivers could contact a CAR T provider for assistance at any time of day.

Patients were admitted for hospital care if they developed Grade ≥2 CRS or ICANS of any grade or if the treating physician determined that other organ toxicity warranted in-hospital care. To minimize the occurrence of high-grade CRS, patients who developed CRS were administered tocilizumab early, when Grade 1 reaction persisted or reached a Grade of ≥2.

Outcomes

Patients treated with CAR-T were followed for a median of 389 days (range, 215–612 days). Two patients received 3 days of prophylactic oral dexamethasone beginning on the day of infusion in a protocol based on ZUMA-1, Cohort 6. Of the 13 patients overall, 3 (23%) did not require inpatient admission during the follow-up period.

CRS developed in 92% of patients (n=12) and persisted a median of 3 days (range, 1–5 days). Events were primarily of Grade 1 (54% of patients; 58% of CRS events). Seven patients (54%) developed ICANS, with no ICANS events of Grade 4. Details of the treatment course, including treatments administered and adverse events, are in Table 5.

Table 5. Treatment Details and Adverse Events[8]

Detail/Event	Outpatients Treated with Axi-cel or Other CAR-T (N=13)
Time from apheresis to cell infusion, days, median (range)	29 (24–54)
Inpatient stays in first 30 days after infusion, days, median (range)	7 (1–14)
Time from infusion to hospitalization, hours, median (range)	96 (11–201)
Hospitalization within 72 hours after infusion, n (%)	3 (23)
CRS, n (%)	12 (92)
Grade 1	7 (54)
Grade 2	5 (39)
Grade ≥3	0
Time from infusion to CRS, hours, median (range)	93.5 (11–201)
Duration of CRS, days, median (range)	3 (1–5)
Tocilizumab for CRS, n (%)	9 (69)
Time from CRS development to tocilizumab infusion, hours, median (range)	24 (1–106)
ICANS, n (%)	7 (54)
Grade 1	3 (23)
Grade 2	2 (15)
Grade 3	2 (15)
Time from infusion to ICANS, days, median (range)	5 (3–17)
Duration of ICANS, days, median (range)	2 (1–3)
Time from ICANS development to steroid administration, hours, median (range)	70.5 (2–178)

CRS=cytokine release syndrome; ICANS=immune effector cell-associated neurotoxicity syndrome.

No patient deaths were considered to be attributable to treatment toxicity. Four patients died from disease progression. The 12-month progression-free survival rate was estimated at 61.9% (95% CI, 32.1%–91.7%), with an overall survival rate of 60% (95% CI, 29.6%–90.4%). At last follow-up, there had been no relapses in the 100-day period after CAR T infusion.

Single-Center Outpatient Administration Study at University of Oklahoma Health Sciences Center[9]

Study Design and Patients

Borogovac, et al. described outpatient administration of axi-cel to 13 patients (12 with diffuse large B-cell lymphoma and 1 with follicular lymphoma). The care center's protocol was designed for outpatient administration; an additional 2 patients received inpatient infusion based on physician assessment of high disease and comorbidity burden.

The treatment protocol included an admission-pending unit for post-infusion observation, daily provider visits on Days 1 to 14, then thrice-weekly visits until Day 28. A telephone line provided 24-hour access to triage nurses.

Outcomes

The overall response rate for the 13 axi-cel-treated patients was 76%, including 9 complete responses and 1 partial response. By 6 months, 8 complete responses were sustained, and 5 patients had progressive disease. Four patients ultimately died of progressive disease and 1 died of infection.

The readmission rate in the first 72 hours after admission for the 13 axi-cel-treated patients was 23% (n=3), with a total of 10 patients (76%) admitted by Day 30. All axi-cel admissions were attributed to fever. Nine patients (69%) developed CRS and 4 patients (31%) developed ICANS. One CRS event and 0 ICANS events were of Grade 3 to 4.

Single-Center Outpatient Administration Study at Johns Hopkins University[10]

Study Design and Patients

In a letter to the editor, Ly et al described outpatient administration of axi-cel (n=29), tisagenlecleucel (n=10), or brexucabtagene autoleucel (n=8) in 47 patients (including 14 [30%] aged ≥65 years and 33 [70%] aged <65 years) between January 2019 and July 2022. Patients received CAR-T therapy in an outpatient setting that included daily monitoring for 14 days by an outpatient unit with extended hours. A 24-hour triage service was provided for direct inpatient admission and toxicity management as needed.

Outcomes

After a median follow-up of 364 days (range, 37–1324), hospitalization rates were 12/14 (86%) in patients aged ≥65 years and 27/33 (82%) in those aged <65 years. Median time to hospitalization was 4 (range, 0–14) days and 2 (range, 0–10) days in patients aged ≥65 and <65 years, respectively. Median duration of hospitalization was 10 (range, 2–29) days and 7 (range, 3–33) days in patients aged ≥65 and <65 years, respectively.

In patients aged ≥65 years, 10/14 (71%) developed CRS and 7/14 patients (50%) developed ICANS. In patients aged <65 years, 25/33 (76%) developed CRS and 9/33 patients (27%) developed ICANS. One CRS event (in a patient aged <65 years) and 6 ICANS events (n=3 each in patients ≥65 and <65 years) were of Grade ≥3. In patients who received axi-cel, all-

grade and Grade ≥3 ICANS were reported in 8/14 (57%) and 4/14 (29%) patients aged ≥65 years and 6/22 (27%) and in 3/22 (14%) patients aged <65 years, respectively.

Multicenter Retrospective Study[11]

A multicenter, real-world study of axi-cel was published and included patients with relapsed/refractory LBCL who received axi-cel as an outpatient infusion. Of 20 reported outpatient infusions, all required admission at median day 1 (range, days 0–8). No additional information, related to toxicity management or monitoring in this subgroup of patients, has been reported.

References

1. YESCARTA® (axicabtagene ciloleucel) [US Prescribing Information]. Santa Monica, CA: Kite Pharma, Inc.; 2023.
2. Leslie LA, Baird JH, Flinn IW, et al. ZUMA-24 preliminary analysis: a phase 2 study of axicabtagene ciloleucel in the outpatient setting with prophylactic corticosteroids in patients with relapsed/refractory large B-cell lymphoma. Poster presented at the 2024 European Hematology Association Annual Congress; June 13-16, 2024; Madrid, Spain
3. Bansal R, Hsu H, Paludo J, et al. Updated trends in real-world outpatient administration of axicabtagene ciloleucel and brexucabtagene autoleucel in relapsed/refractory non-Hodgkin lymphoma. Poster presented at the 2024 European Hematology Association Annual Congress; June 13-16, 2024; Madrid, Spain
4. Bansal R, Paludo J, Holland A, et al. Outpatient practice pattern and remote patient monitoring for axicabtagene ciloleucel CAR-T therapy in patients with aggressive lymphoma. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting; June 4-5 2021; Abstract 7554. DOI: 10.1200/JCO.2021.39.15_suppl.7554
5. Bansal R, Paludo J, Hathcock MA, et al. Outpatient practice pattern for recently approved CAR-T in patients with lymphoma and multiple myeloma. *Blood*. 2022;140(Suppl 1):2399–2401. DOI: 10.1182/blood-2022-167187
6. Battiwalla M, Egloff SA, Blunk B, et al. The Patient Journey and Treatment Outcomes Comparing Inpatient Versus Outpatient Axicabtagene Ciloleucel in Non-Hodgkin's Lymphoma - a Large, Multicenter Study. Poster presented at the 66th American Society of Hematology (ASH) Annual Meeting & Exposition; December 7-10, 2024; San Diego, CA.
7. Kirby S, Hoda D, Hunter B. Successful outpatient treatment and monitoring following administration of various anti-CD19 chimeric antigen receptor therapies in B-cell lymphomas. *Blood*. 2022;140(Suppl 1):10812-3. DOI: 10.1182/blood-2022-168207
8. Dholaria B, Mehraban N, Baer B, et al. Feasibility of outpatient administration of axicabtagene ciloleucel and brexucabtagene autoleucel using telemedicine tools: the Vanderbilt experience. *Br J Haematol*. 2022;198(6):1073-1075. DOI: 10.1111/bjh.18339
9. Borogovac A, Keruakous A, Bycko M, et al. Safety and feasibility of outpatient chimeric antigen receptor (CAR) T-cell therapy: experience from a tertiary care center. *Bone Marrow Transplant*. 2022;57(6):1025-1027. DOI: 10.1038/s41409-022-01664-z
10. Ly A, Sanber K, Tsai HL, et al. Outpatient CD19-directed CAR T-cell therapy is feasible in patients of all ages. *Br J Haematol*. 2023;203(4):688-692. DOI: 10.1111/bjh.19090
11. Nastoupil LJ, Jain MD, Feng L, et al. Standard-of-care axicabtagene ciloleucel for relapsed or refractory large B-cell lymphoma: Results from the US Lymphoma CAR T Consortium. *J Clin Oncol*. 2020;38(27):3119-3128. DOI: 10.1200/JCO.19.02104
12. ClinicalTrials.gov. Study of Axicabtagene Ciloleucel Given With Steroids In Participants With Relapsed Or Refractory Large B-Cell Lymphoma (ZUMA-24) (NCT05459571). Available at: https://clinicaltrials.gov/ct2/show/NCT05459571 [Accessed November 2024]

Abbreviations

AE=adverse event
CAR=chimeric antigen receptor
CRS=cytokine release syndrome
DLBCL=diffuse large B-cell lymphoma
ECOG= Eastern Cooperative Oncology Group
EMP=early management period
FL=follicular lymphoma
HGBL=high-grade B-cell lymphoma
ICANS=immune effector cell-associated neurotoxicity syndrome
ICU=intensive care unit;
IPI=International Prognostic Index
IQR=interquartile range;
LBCL=large B-cell lymphoma
LMP=late management period
LOS=length of stay;
MCL=mantle cell lymphoma
MM=multiple myeloma
NE=neurologic events
NHL=non-Hodgkin lymphoma
PMBCL=primary mediastinal B-cell lymphoma
RPM=remote patient monitoring
R/R=relapsed/refractory
SAE=serious adverse event
SPD=sum of the products of the diameter
TFL=transformed follicular lymphoma
WBC=white blood cell

Product Label

For the full indication, important safety information, and Boxed Warning(s), please refer to the YESCARTA® (axicabtagene ciloleucel) US Prescribing Information available at: https://www.gilead.com/-/media/files/pdfs/medicines/oncology/yescarta/yescarta-pi.pdf

Follow Up

For any additional questions, please contact Kite Medical Information at:

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FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉ MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or www.accessdata.fda.gov/scripts/medwatch

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